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授与した学位	博　　士
専攻分野の名称	薬　科　学
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学位授与の要件	医歯薬学総合研究科　薬科学専攻 （学位規則第４条第１項該当）
学位論文の題目	Application of the 1H-qNMR method to quality assessments of herbal drugs, rhizomes of *Acorus calamus* and *A. gramineus* and the effects of their constituents on *in vitro* acetylcholinesterase activity　（1H-qNMR 法のショウブ属植物根茎由来生薬の品質評価への応用とアセチルコリンエステラーゼ *in vitro* 活性に対する含有成分の効果）
論 文 審 査 委 員	教　授　　好光　健彦　（主査） 教　授　　澤田　大介　　准教授　　神野　伸一郎

学　位　論　文　内　容　の　要　旨

This thesis describes the application of quantitative NMR (qNMR) method as a simple and easy method to quantitate main constituents from well-known medicinal herbs, *Acorus calamus* and *A. gramineus*. The experimental parameters of the qNMR measurements were optimized for the main constituent, β-asarone, isolated from *Acorus* rhizomes. The established qNMR method was then applied to estimate purities and stabilities of the isolated main compounds, β-asarone, α-asarone, and asaronaldehyde. Furthermore, the linearity, accuracy, and precision of the qNMR method were also investigated by using the β-asarone pure sample. Based on these, the levels of these main asarone-related compounds in *Acorus* products were estimated by the qNMR method and compared with the results from the conventional chromatographic method, HPLC. The effects of crude *n*-hexane extract from *Acorus* products and their principal constituents on AChE (acetylcholinesterase) enzyme were also evaluated in *in vitro* assays, to show the potent inhibitory effect of β-asarone, and an enhancing

effect of eudesmin A. As a conclusion, the established qNMR method was a simple and useful method for the estimation of the purities of the isolated compounds and the levels of the main constituents of *Acorus* rhizomes, and revealed the roles of the constituents in the effects on AChE.

The thesis is organized as follows: Chapter 1 describes the introduction of the qNMR method and medicinal usages of *Acorus* rhizomes. Chapter 2 narrates the optimization of the qNMR method parameters and preparation of the principal constituents from *Acorus* rhizomes. Then, the purity and stability of each of the main asarone-related compounds were elucidated. The accuracy, precision, and linearity were also exhibited in the quantitative analyses when using the method with the established parameters. The levels of the main asarone compounds in the *Acorus* products were then estimated by the qNMR measurements, and the results were compared with those from the HPLC method, to reveal respective superiorities. Chapter 3 describes the evaluation of the AChE inhibitory effects of *Acorus* samples and the contribution of their principal constituents. In addition, the estimated inhibitory effects on AChE and the AChE enhancing effects of eudesmin A, a first isolated compound from *Acorus* species, were also presented. Chapter 4 outlines the experimental conditions, methods, and instruments used in this study.

論 文 審 査 結 果 の 要 旨

当該論文は、ショウブ属植物根茎に起源をもつ生薬薬効成分の定量解析法の開発並びに含有主成分の生物活性評価に関する研究成果を論じたものである。本研究では、有機化合物の構造解析に汎用される核磁気共鳴スペクトル法を定量解析に適用することによって、従来法の精確さを上回る上記生薬主成分の定量法を確立することに成功しており、十分な進歩性と応用性が認められる。本研究における核磁気共鳴スペクトル定量解析手法の有用性の確立は学術的にも意義深く、関連研究領域の進展をもたらすことが期待される。また、上記生薬の主成分であるフェニルプロパノイド β-asarone が顕著なアセチルコリンエステラーゼ阻害活性を示すことも明らかにされており、ショウブ属植物根茎由来生薬の薬理活性と含有成分の関係を示唆する知見も興味深い。以上、博士論文として十分な質と量を備え、評価基準を満たしていることから、当該論文を本研究科の博士学位論文としてふさわしいものと認める。